

## The Demon of the Federation\*

By ALBERT I. MENDELOFF

THE ANCIENT GREEK had his personal demon—a distilled essence of what he really was, a disembodied spirit which was thought to accompany him, always hiding behind and a little above him, never visible to its owner, but clearly discernible to every stranger.† For those of us brought up in the twentieth century the analogy of the demon with the idea of self is readily appreciated, as an attempt again to deal with this perennial problem of self-knowledge, identity, purpose and achievement.

The early Greeks were not "organization men"; I can find no mention of the demon of any Greek organization, but many of the great Attic writers tried to point out that notions of identity held by their compatriots were wrong—so Aeschylus tried to convince the Athenians that their narrow city-state interests were blinding them to the larger Panhellenic allegiance they refused to acknowledge. Nevertheless, every active group does need to have an image of itself to display to the world, an image fused of its purposes and its ideals, an organizational demon. Our organization is not exempt from such a requirement. Particularly in view of this past year of financial and constitutional turbulence, the American Federation for Clinical Research must, whether it likes it or not, answer the classic questions, "What are we? For what purpose do we exist?"; it must produce from somewhere a demon for all to see.

From ancient Greeks to Young Young Turks is a short trip for the imagination; there is such a demon available. From the beginning the Young Young Turks attempted to create a group whose

distinction lay in its simplicity: an association designed to offer a forum for young investigators, to restrict only the age and not the number of its members and to make admission to its ranks relatively easy. Our organization grew very slowly, and its operating costs were minimal. With the entry of the United States into World War II, the organization almost died, only to be reborn at the end of that war with a vigor and numerical growth of remarkable proportions. Under the paternal and avuncular care of the American Society for Clinical Investigation, its own officers gave it cohesion and forceful leadership as it grew into what is today the largest organization for clinical investigation on this continent.

One cannot but be astonished that an organization so unpretentious, so nonexclusive, and so junior by constitutional law could attract so many members. There are at least two reasons for this attraction. For the young investigator, membership in the Federation apparently fulfills his need for being identified with others who share his interests and purpose. As he listens to papers being presented at meetings, as he leafs through *Clinical Research*, he feels some quickening of the spirit, translates his personal acquaintanceship with the speakers or authors, his contemporaries, into a wish to emulate or surpass their efforts. The organization encourages him to do so by placing as few barriers as possible in the aisle to the speaker's rostrum, provided only that he have something worthwhile to say.

A second feature of this group is that it does not unceremoniously drop its members when they reach the advanced age of 41. Rather, it enables them, as senior members, to perpetuate their relationship to the younger men for whom the Federation was created, by actively encouraging and stimulating investigative careers. Again, no barriers are organizationally created which might prevent this healthy symbiosis. It is this continuity of partnership which is largely responsible for the rapid growth of the Federation.

Since 1950 the rate of growth has been of

\*Presidential address, read before the National Meeting of the American Federation for Clinical Research, Atlantic City, New Jersey, May 3, 1959.

†This is the author's interpretation, of course. "Daemons," good and evil, appear throughout classical and medieval literature. I have selected the kind of demon most suitable for this essay from the splendid collection of "daemons" available in the writings of the past.

the order of ten to twelve per cent per year. According to the report<sup>1</sup> of the Consultants on Medical Research and Education to the Secretary of Health, Education and Welfare, there are at present some 20,000 professional research workers in medical fields in the United States; of these 20,000, nearly 3,500, or fifteen per cent, belong to the Federation. This same report, which I recommend all of you to read, anticipates a total working force of 45,000 professional medical investigators ten years hence; if the same percentage of these people continues to join the Federation during this decade, our organization will number some 7,000 members made up of many diverse disciplines. Should members reaching senior status continue to stay interested enough to retain their senior memberships, the total may well be higher. We can anticipate local research clubs in many areas not now boasting them, as well as in the new states of Hawaii and Alaska. There will be marked changes in the distribution of members among the geographic sections; there may well be six or eight such sections rather than four, and the number of abstracts submitted to meetings will double or triple, forcing the sections to have either more frequent general meetings or to have at each meeting combinations of general and specialty programs such as we now present nationally here at Atlantic City.

In the face of this remarkable demonstration that so many young people wish to affiliate themselves with an organization which confers so little prestige on its members as members, your officers over this past year have tried to polish up the demon of the Federation for all to view with pride. It may be represented by the three principles listed below:

#### *The Demon of the AFCR*

1. *To promote and encourage original research in clinical and laboratory medicine.*
2. *To welcome as members and provide an accessible forum for young persons engaged in such research.*
3. *To set no numerical limit to membership.*

One cannot but admire the foresight of that small group of men who founded the Federation in 1941. In order to maintain the demon

they created and in order to gear the organization for the enormous demands that will be made upon it in the next decade, your present officers have worked on three major projects. First, we have felt that a complete overhauling of the constitutional machinery handed down to us from our predecessors must be undertaken immediately. Accordingly, we have completed a revision of the constitution. Second, the burgeoning membership has made it urgently necessary that we recast the form of our Journal to trim our costs of publication. Accordingly, we have changed the format and typography of future issues of *Clinical Research*. In so doing, the organization has been placed on firmer financial grounds. And third, the rapid growth of the membership and the fact that one-fourth of our regular members change addresses each year has made it impossible for any person trying to fulfill his duties in academic medicine to also give up the time necessary to serve effectively as the Secretary-Treasurer of this expanding colossus. Consequently, we have this year established a National Office in New York City with an Executive Secretary and two full time secretaries to carry out the demanding duties of coping with membership and publication problems, thus allowing the Secretary-Treasurer time to breathe and think.

The number of man-hours required to make these radical revisions in our machinery without compromising our demon has been staggering; I cannot thank enough the members of the Council, the Editor of the Journal, and your new President and the Secretary for their devoted efforts in behalf of the organization. We are grateful to the entire membership for paying so willingly the extra assessment this year and to those individual members who took the time to write me so many thoughtful letters regarding constructive ways of dealing with our problems. If through these changes we can preserve our demon, and at the same time make it possible for the Federation to meet the demands the young investigators of this country apparently want it to bear, these efforts will have all been well spent.

#### REFERENCE

1. The Advancement of Medical Research and Education. Washington, D. C., U.S. Government Printing Office, 1958.

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## Communication as a Problem of Science\*

By ALBERT SEGALOFF

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A MAJOR PROBLEM of science is the communication of research findings so that they can be used for the increase of general scientific knowledge. In our complex scientific community, an important means of communication between scientists is, of course, informal discussion. This then gives way to more formal discussions such as the presentation of communications at meetings.

The first problem in the way of discussion is that of a common language. By this I do not mean French, German, Russian, Sanskrit or Chinese since we are all speaking English. The language to which I refer is the language of science. As scientists, we all tend to speak in the specialized terms of our own fields. If our results are to be meaningful to more people, some means must be found to express our scientific thoughts in a common language. If one looks at the program being presented today, it is obvious that men are presenting distinguished scientific papers but in vastly differing fields of endeavor, all of which come under the wing of that very small segment of science which is clinical research. On the one hand, we have a paper presented by a chemist on the incorporation of radioactive substances into various hormonally-active steroids by tumors. On the other hand, we have a clinician presenting a paper on clinical physiology. These people speak a common language, English, it is true, but not a common scientific language.

It may be possible that some sort of translation scheme might be the solution—that is, having someone who is conversant with more than one field attempt to reduce the scientific language to more understandable terms for the people whose major interests lie in different areas. Of course, it is also possible to split the group into smaller sections which would permit the presentation of more communications, but to a restricted audience. I do not believe that either of these alone is the best solution. I think it best that we combine both of these approaches. First, as most of our authors are trying to do,

we should express results in terms as understandable as possible to the audience, each author acting as his own translator by the utilization of a graphic presentation of pertinent chemical structures and physiologic events. These make the results more understandable to the novice in the particular field. Second, we might also add multiple small meetings to be attended only by those conversant with a specific field and thus permit presentation of highly technical communications.

But the overall problem of communication which confronts science is much graver than this. It involves the huge bulk of the world's scientific literature and its ever increasing size due to the pressure for research in the physical sciences. The demand for better things for better living, bigger and better weapons of offense and defense, better health and longer life has also produced a pressure on the biological sciences. The mass of literature has become so vast that it is impossible for any individual to become familiar with it in any field however restricted.

Since clinical research is only a restricted area of biology, I thought that it would be interesting to confine my calculations and discussion to the problem posed by the biological literature. The figures which I have been able to obtain in my attempts to answer this question are astounding and are so monumental that they are difficult to visualize. I will, for the present, ignore the many books and other types of communications and concentrate entirely on periodicals. I will also consider the entire possible biologic literature rather than attempt, as others have done, to winnow out that which is of "research caliber." It has been estimated that there is a minimum of 20-25,000 periodicals being published in the world annually carrying biological literature. Various additional estimates place the number of articles at somewhere between 50 and 150 per year per journal. Let us for the sake of comparison simply take an average of 100 articles per year and the low figure of 20,000 journals. If we assume that each journal puts out an average annual thickness of three inches, these journals if stacked would make a pile one mile high. This mile high stack of journals would contain some 2 million articles on biology!

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\*Presidential Address read before the annual meeting of the Southern Society for Clinical Research in New Orleans, Louisiana, January 28, 1958.

It is true that from the point of scientific advance, many of these articles are worthless. As a matter of fact, I think I would not be too facetious if I were to say that, as additions to scientific knowledge, most of the articles are valueless. If one particular journal or group of journals were singled out for widespread dissemination, limiting distribution of others, then the problem of selection would develop. In the field of endocrinology, my favorite example of the risk entailed in such selection harks back to the work of Dr. Adolph M. Hanson in Faribault, Minnesota, where, supported only by his practice, he was able to solve a very major problem of parathyroid function and to prepare an extract which worked in parathyroidectomized dogs. This was published in *Military Surgeon*, which is not a biological research journal, and so did not receive general recognition for some time. Thus, it is my feeling that the risk is too great to try to aim at a system for dissemination of biological data that is anything less than complete.

Biological Abstracts, a joint effort by a great many biologists, has fallen far short of an ideal goal, and last year, despite its great cost and the effort that has gone into it, succeeded in publishing and indexing the abstracts of only some 36,000 articles. The Russians were dissatisfied with the availability of abstracts in the biological field and in 1956 started their own abstracting service which abstracted and indexed 106,000 articles in its first year and is still not complete, though this performance is three times that of Biological Abstracts. It would appear that in biological abstracting they have beaten us, but not quite as badly as they did in getting a satellite into space.

This brings us to the problem of indexing the literature. The adequacy of the index depends on its completeness. Complete indexing requires not only a system of indexing but highly skilled people to carry it out. It has been estimated that each abstract should generate an average of more than four and often, depending upon completeness, as many as ten or twenty index entries. This accounts for a gargantuan number of index entries. For example, our 2 million biological abstracts would then generate a minimum of 8 million index cards. Interestingly enough, these theoretical 8 million punch or index cards would make a pile almost exactly as high as the pile of journals, approximately one mile. Of course, the better the index, the greater the number of index cards.

I do not know how you feel in this machine

age, but I shall never forget my first impression of the I.B.M. punch card sorter. My eyes popped at the rapid rate at which this marvel of the electronic age could sort cards accurately according to little holes punched in them. A little sober reflection will show you that the task we face is so immense that even the early punch card sorters are just not adequate. For example, the I.B.M. punch card sorter which we have in our institution is a standard one which will sort and count cards at the rate of 425 cards per minute. It will, however, sort only one of the 80 columns at a time. The manufacturers have improved such equipment and the best machine of this type will sort cards at the rate of 1,000 per minute. Assuming that we have a code, to find an individual set of cards it would be necessary to sort through the entire lot—all 80 columns—some entries being located with few sortings and others only after many more. It would take a man working at this advanced single column sorting machine 5 days a week, 8 hours a day, with no coffee breaks, a full year to sort four million cards. This really means that every day this man and his machine could sort the biological index cards one half as fast as they are being generated. Of course, there are other aids to the problem if one is looking for just a single piece of information. One can have the machine working on two shifts, and that would just keep abreast of the new index cards. Obviously, this is not the solution. I am using it only to illustrate the fact that the simple I.B.M. machine with its apparently colossal rate of sorting is simply not adequate to the task. This does not take into account the number of people nor the additional machines which would be required to produce the abstracts and the index cards. The obvious initial answer to this problem is to have signal codes of categories which would subdivide the material so that it will not be necessary to sort through the data on rhinoceri if one needs only the information on frogs. This again poses more problems, such as cross-indexing, which would generate more and more punch cards. The next step would be to use a statistical sorting machine which can sort more than one column at once. Ideally, we would set up a punch card system which is filed according to broad areas; then the cards for the specific finding within the area of study are sorted on a statistical sorting machine. This would enable one to keep up in a more adequate manner if all the material were gathered to feed into the machine.

There is one other new, supplemental system



which is available. The Eastman Kodak Company has an extremely interesting device which combines optical scanning at less capacity than standard punch cards with the use of small negatives on which documents can be copied and then converted into legible data. These mini-cards are then filed on "sticks" from which they can be retrieved for further use. At the moment this system is not generally available but is being used by the originators and a few government agencies.

This then brings us face to face with the problem. We have created a Tower of Babel. I realize that the solutions that previously have been offered by others have not found acceptance. The solution for the growing mountain of literature and its inaccessibility might best be solved by a combination of methods. First, most of our scientific journals should become abstract journals in which one publishes an abstract of his data and also codes it according to a large universal indexing system which would be available. This, I believe, would raise the quality of abstracting as well as the adequacy of the indices since this skilled job would be, as it were, the means of selling one's data and ideas. The abstract would best be written by the one who carries out the studies, and he should be the best one to decide under what headings the abstract should be catalogued. The machine code would then furnish for the first time a truly universal language of science, since the punch card would be identical whether the man who coded the material spoke Chinese, Russian or English! Second, the manuscripts containing the original data would be deposited in a central depository and copied on a file suitable for photographic reproduction.

The indexing should be placed either on the most advanced punch card system or probably, because so much data would be involved, on one of the electromagnetic memory devices. Then as scientists doing research in individual fields read the journals containing the abstracts, they could get a micro-card reproduction of the original manuscript at modest cost. In addition, the central institution where the manuscripts and data are processed could be the center for the compilation of available data from the indices, the abstracts and the original manuscripts. These could then be compiled and made available either

as reviews or as individual data to qualified investigators who when necessary, could obtain the original data on micro-cards. Third, all the abstracts translated into several languages, plus the abbreviated index for the final retrieving of the data, should be on mini-cards from which prints could be made.

Thus, the universal language of science would, under this scheme, be the code language of the machine. The next step would be the translation of the abstracts into the several written languages and, finally, translation of the completed manuscript only when it seems advisable on the basis of the data in the code and the abstract.

A complete cooperative system such as this would solve the data problem for the future, but what about the past and present compilation of reviews which can be assimilated by the working scientist? This can only be handled by making literature compilation, translation and coding an attractive profession. It would require a great deal of training to make individuals skillful enough to carry out this difficult task. This should be on a par in remuneration and recognition with our best professions or it would not work.

This, of course, is costly, but no more so than letting the data of research of potential importance to human biology be buried forever in inaccessible places, or to waste even more money in unnecessary duplication of the efforts of others rather than exploring with the certain knowledge that you are in virgin territory. Thus, we would set the stage to make it possible for individual investigators to be more thoroughly versed in their own fields and to make data that are more detailed than are now in the journals available for those who are interested, without wasting journal space. Although this would be expensive, it need not be excessively expensive, since the actual abstracting and indexing would be done by the authors who could do it most adequately. I recognize that this would require a tremendous amount of cooperation and probably must be done on a world-wide scale to be successful. However, I am firmly convinced that only such a world-wide effort will bring order out of the chaos which now exists when one attempts to survey adequately the available scientific literature in any field.

## NOTICES

### Action of the Council

At the meeting of the Council of The American Federation for Clinical Research held in Atlantic City on May 2, the following actions were taken: (1) The Secretary-Treasurer was empowered to screen all applications for membership and to accept in the name of the Council those applications whose evidence appears to be incontestable and to circulate to the Officers and the indicated Section Chairman any application in which there is any question as to the applicant meeting the Constitutional requirements for membership. The Secretary noted that 376 new Regular Members had been processed in 1958-59, and 114 had been advanced to Senior Membership. (2) Subject to certain stipulations, the Council authorized preparation of a membership card to be distributed to members as they pay their dues and assessments in 1960. (3) It was noted with satisfaction the admission of 16 new Corporate Members as of 1959, increasing the Federation's annual income from Corporate Memberships from \$6,500 to \$10,500 annually. Council directed that acknowledgment of the participation of Corporate Members and their contribution to the Federation shall be published henceforth in each issue of *Clinical Research*. (4) The Council affirmed a previous decision that all future issues of *Clinical Research* be produced by author-composition, photo-offset printing insofar as abstracts and Roster copy are concerned; that each issue of *Clinical Research* henceforth carry an Abstract Form with instructions for the use of members preparing abstracts; that the issue normally published on September 1st, is to be redesignated the August issue to be published August 1, 1959, to contain the Roster in alphabetical form. (5) Certain recommendations of the Publication Committee were adopted as follows: (a) That the Federation approve and accept an annual basic publisher's office cost for *Clinical Research*, the precise terms of which are to be negotiated with the publisher. (b) That further arrangements for the subsequent publication of the Journal shall be negotiated after appearance of the August issue. (6) Dr. S. Richardson Hill was elected a member of the Publication Committee succeeding Dr. Arnold S. Relman. (7) The text of the proposed, revised Constitution was approved, and it was to be presented to the Membership at the 1959 Annual Business Meeting of the Federation, and to lie over for final approval at the 1960 Annual Business Meet-

ing of the Federation, in accordance with Article VIII of the existing Constitution. (8) The draft of a proposed set of By-Laws to be adopted by the Federation after it has adopted the proposed, revised Constitution was reviewed, and the substance of these By-Laws subject to revision by Legal Counsel was approved. (9) The administrative contract with James E. Bryan and Randall Norris was renewed for a two-year period. An expression of gratitude to Miss Lila Mitchell for her long and valuable association with the Federation was unanimously voted. (10) A projected tentative budget for 1960, as proposed by the Executive Committee was adopted, and the Council further directed that an assessment of \$2.50 per member be levied for 1960 for Regular Members of the Federation, and that an assessment of \$5.00 per member be levied for 1960 for Senior Members, these assessments to be billed with and in addition to the regular dues for 1960, which will be \$5.00 per member. The Council also directed that all members serving as internes, residents and fellows be exempted from these assessments. (11) The Council adopted a policy that the Federation should increase its reserve funds until such funds are equal to one year's budget of normal Federation operations. (12) A gift of \$50.00 to the National Society for Medical Research for the current year was authorized. (13) The Executive Committee was authorized to make all necessary arrangements for the Scientific Meetings in 1959-60. (14) In accordance with Article III, Section 6, of the Constitution, the Council elected Dr. William W. Stead, President of the Federation for 1959-60; Dr. Arnold S. Relman was elected Vice-President of the Federation for 1959-60.

George E. Schreiner  
Secretary-Treasurer

### Change of Address

To ensure prompt and continuous receipt of the Journal, subscribers should report changes of address to the Publisher (Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, N. Y.) at least 30 days before the publication date of the next issue. Both the subscribers new and old address should be given. *Members of the Federation* should at the same time supply a duplicate of this information to the National Office (American Federation for Clinical Research, 250 West 57th Street, New York 19,

N. Y.) so that records and roster can be kept up to date and official notices properly directed.

### National Research Council

The annual meeting of the National Research Council was convened by President Bronk at 2:00 p.m., March 19, 1959. Many of the problems encountered in efforts to plan, guide and subsidize research on both a global and national scale were discussed in this first plenary session by Detlev Bronk, Warren Weaver, J. George Harrar, Clyde K. Kluckhohn and Donald G. Marquis. Of particular interest was a lively discussion of the planning and conduct of our research programs in foreign countries.

The topic for the evening program was "Means and Patterns for the Support of Scientific Research." Here the discussion was led by James R. Killian, Alan T. Waterman and James A. Shannon. Great interest was shown in the forward-looking plans of the U. S. Public Health Service to broaden the base and latitude of subsidy programs in order to best serve the changing climate of research. In this connection it is noteworthy that the large number of scientists who receive support from other granting agencies were, with wholesome envy, also eager to hear of the tentative details from Dr. Shannon. It has been hoped that the U.S.P.H.S. plans would serve as a model for other agencies.

On the morning of March 20 the topics of the previous afternoon and evening were further developed in each of two simultaneous sessions. Here facets of innumerable variety were considered. Particularly since the United States has a shorter background of experience than many in the affairs of other nations and their local customs,

it was reassuring to learn of the rapidity with which our scientific community is learning to work effectively abroad; the NRC merits special recognition in this achievement.

In the afternoon each Division in the NRC had its meeting. Of the many things considered by the Division of Medical Sciences, the following are of the most general interest. The National Research Council fellowship program is undergoing revision whereby fewer awards will be made, and new patterns of the fellowship programs are being explored. The Division is very actively engaged in bioastronomics with the immediate aim of determining biological prerequisites for placing man in space. Facilities and personnel for the training of the large number of psychiatrists and psychologists needed are being reviewed. This matter has been of special concern because of the disproportionately small number of medical school graduates who are entering this area of special work. Finally, it is hoped that a greater number of younger men be asked to participate in the work committees of the Division of Medical Sciences. At present, only one per cent of the Division's complement is under the age of 36 years.

It is an honor for our Society to be represented on the National Research Council and a testimony to the role of The American Federation for Clinical Research in the present growth and development of American science.

William J. Harrington  
Representative to the  
National Research Council

### New Research Tools

The information reported here is obtained

### New Procedure for Preparing and Submitting Abstracts

By order of the Council, all abstracts henceforth will be composed by the author and reproduced by photo-offset process directly from the author's typed composition.

In this issue of *Clinical Research*, and in each subsequent issue, you will find "Abstract Reproduction Forms" which must be used by authors in submitting manuscripts for reproduction. (Removable forms will be found in the front advertising section of this issue.)

(NOTE that in instruction No. 2 of the Abstract Reproduction Form it is erroneously stated: "Leave no top or bottom margin . . ." This should read: "Leave no top or left hand margin . . .")

All members submitting abstracts are requested to use these forms with due regard to the rules and requirements set forth on both sides of the forms.

from manufacturers. All notices and inquiries should be addressed to **New Research Tools Editor, Samuel N. Turiel & Associates, Inc., 430 N. Michigan Avenue, Chicago 11, Ill.** Include name(s) of the manufacturer(s).

- **New high speed decade scaler (10<sup>6</sup> CPM)** with 55 minutes preset period maximum. Nuclear Measurements Corp.

- **Boron trifluoride neutron detectors** available in several lengths, to be used directly with one-millivolt scaler. Nuclear-Chicago Corp.

- **Fluorescein isothiocyanate** in ampule (500 mg.) and bulk amounts (1 and 5 Gm.) for selective staining of antigens. Nutritional Biochemicals Corp.

### Obituary

The National Office has been notified of the death of the following member:

Dr. Lincoln Godfrey, Jr.  
Philadelphia, Pa.

### Members Lost to the National Office

The current address of the following members is unknown:

	Former Address
Lt. Col. Marion E. McDowell, M.D.	U.S. Army Tokyo Army Hospital A.P.O. 500 San Francisco, Calif.
Frank A. Montmorency, M.D.	Department of Urology Wayne State University College of Medicine 1401 Rivard Street Detroit 7, Mich.
L. O. Standaert, M.D.	Department of Internal Medicine University Hospital Ann Arbor, Mich.

It would be appreciated if any member knowing the current address of any of the above members would write to: American Federation for Clinical Research, 250 West 57th Street, New York 19, N. Y.

THE AMERICAN FEDERATION FOR CLINICAL RESEARCH was organized in 1940-41 by Dr. Henry Christian and a group of surviving charter members of the American Society for the Advancement of Clinical Investigation "to stimulate among young men a persisting interest in investigation in clinical and allied medical sciences."

"Anyone under the age of 41 who has completed and published a meritorious investigation in clinical medicine or allied sciences shall be eligible for membership."—*from the Constitution*



1959-60

## SECTION MEETINGS

### American Federation for Clinical Research

#### MIDWESTERN—Chicago

DATE: NOVEMBER 5, 1959  
(Thursday) 9:00 A.M. - 5:00 P.M.

PLACE: THORNE HALL, AUDITORIUM  
Northwestern U. Medical  
Campus,  
Lake Shore Drive and  
Superior Street.  
(Headquarters Drake Hotel)

ABSTRACTS: Must be mailed by  
September 5, 1959, to:

*William J. Harrington, M.D.,*  
Department of Internal Medicine,  
Washington University School of Medicine,  
600 South Kingshighway,  
St. Louis 10, Missouri.

*(Abstracts may not be withdrawn after  
September 12)*

#### EASTERN—New York

DATE: DECEMBER 10, 1959  
(Thursday)  
9:00 A.M. - 12:00 NOON  
2:00 P.M. - 4:30 P.M.  
8:00 P.M. - 9:30 P.M.

PLACE: THE AUDITORIUM,  
ALUMNI HALL,  
New York University-Bellevue  
Medical Center,  
First Avenue and 31st Street,  
New York, N. Y.

ABSTRACTS: Must be mailed by  
October 19, 1959, to:

*Daniel S. Lukas, M. D.,*  
New York Hospital—Cornell Medical Center,  
525 East 68th Street, New York 21, N. Y.

*(Abstracts may not be withdrawn after  
October 26)*

#### SOUTHERN—New Orleans

DATES: JANUARY 21, 1960 (Thursday)  
9:00 A.M. - 5:00 P.M.  
JANUARY 23, 1960 (Saturday)  
9:00 A.M. - 12:00 NOON.

PLACE: HOTEL JUNG

ABSTRACTS: Must be mailed by  
October 30, 1959, to:

*John C. Rose, M.D.,*  
Georgetown University School of Medicine,  
3900 Reservoir Road, N. W.,  
Washington 7, D. C.

*(Abstracts may not be withdrawn after  
November 9)*

#### WESTERN—Carmel, California

DATES: JANUARY 27, 1960 (Wednesday)  
1:30 P.M. - 5:30 P.M.  
JANUARY 28, 1960 (Thursday)  
9:00 A.M. - 12:30 P.M.

PLACE: GOLDEN BOUGH THEATRE  
(Headquarters LaPlaya Hotel)

ABSTRACTS: Must be mailed by  
November 2, 1959, to:

*Gerald T. Perkoff, M.D.,*  
Salt Lake General Hospital,  
Department of Medicine,  
175 East 21st Street, South,  
Salt Lake City, Utah.

*(Abstracts may not be withdrawn after  
November 9)*

The chairman of the national meeting of the Federation and the chairmen of the various section meetings sponsored jointly by the Federation and by The Society for Clinical Investigation were asked to submit comments concerning their respective sessions. As can be seen, these comments include both detailed summaries of the proceedings and general interpretive remarks. No specific ground rules have been set by the editors for these comments, but it is hoped that such reviews will provide a useful perspective of an important Federation activity.

### **General Meeting**

Promptly at 9:15 a.m. on the morning of May 3, 1959 the Scientific Session of the General Meeting began. The business session beforehand had gone smoothly, and a large audience had accumulated in the Steel Pier theatre by the beginning of the program. Throughout the morning the audience continued to remain very large, taxing the capacity of the theatre.

Generally speaking, the papers proved to warrant the confidence placed in them by the President—they were of general interest, well presented, and competently discussed. Only one speaker went overtime; three finished with several minutes to spare. Discussion was of the tandem type, the superiority of which has been well demonstrated in these meetings previously. The paper by Dr. Sevelius of Oklahoma City evoked the most vehement critical attack; the aplomb displayed by Dr. Sevelius in his responses was so striking that the audience was constantly laughing, providing a relaxation of tension greatly appreciated by the officers.

Almost all of the subsection specialties were represented by the papers on this National Program, but one paper—the demonstration of the technique of transspinous cavography by Dr. Schobinger, employing a radiologic method developed by a surgeon to show deformities of the vena cava and vertebral veins caused by disease processes—could not be classified into any specialty. We need more papers of this type.

With the increasing complexity of techniques used in clinical research, and the narrowing of focus of such techniques on minute aspects of problems, it becomes more and more urgent that at least a portion of the National Program maintain a broader outlook on the entire field of investigation. Since the President can only choose from the abstracts submitted, I should like to

urge the members of the Federation to submit abstracts properly qualifying under these general rules rather than hold them back because of a false pride or fear that they are not "specialized enough."

*Albert I. Mendeloff, M.D.*  
Sinai Hospital  
Baltimore, Maryland

### **Section I**

The Cardiovascular Section met in the Carolina Room of the Chalfonte Hotel. Apart from some difficulty about microphones and a pointer, the meetings seemed to go smoothly. When this particular auditorium is full, it is next to impossible for members of the audience in the rear of the room to hear what is being said at the front. This room should be equipped, in the future, with at least four microphones on the floor and a breast-type microphone for the speaker. Also, a pointer of some sort should be provided for the speaker. There was insufficient time to repair the difficulties before the meeting.

The papers were, with very few exceptions, of an unusually high order. There was a great deal of material from which to select, and I think it would have been possible to make up another program of the same length if not quite of the same quality. I should say that there were at least six additional papers which we had to reject rather arbitrarily. In general, the presentations were well arranged, and the preparations for them were excellent.

I think it would be desirable if the co-chairman of the sessions could have some voice in the final choice of the program. With time so pressing when the abstracts begin to come in, I have no ready suggestions to offer unless the chairman and co-chairman happen to live fairly close together. Finally, I believe the system of sectional meetings represents a very real advance in program planning, particularly now that both societies participate in them. For certain material, a sectional meeting is actually better than the general session, and I have heard it said more than once that some investigators would now prefer to present their material before the sectional audience than before the general one. If this view grows, it may actually begin to make the general meetings less attractive, but I do not think that this possibility need give any great concern at the moment. There is also the strong possibility that the cardiovascular section will

very shortly outgrow the Carolina Room and that a larger auditorium will have to be found.

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## Section II

The principle of sectional meetings on restricted topics can be criticized because of the need for a broad outlook by the clinical investigator regardless of how restricted his research program may be. Nevertheless, a number of factors have developed which make the sectional meetings very useful. The first of these is a purely mechanical one of housing a large audience, amply attested to by the great crowd in the Steel Pier Theatre at all of the combined sessions. In a way, the afternoon meeting of the Metabolism and Endocrinology Section gave even more dramatic testimony. The Vernon Room of Haddon Hall furnished, in the not too distant past, a meeting place of adequate size for the combined groups. At our afternoon session, the Vernon Room was filled to comfortable capacity by the metabolism section alone. Both the magnitude of the group interested enough to give careful attention to the presentations and the many abstracts from which only 15 could be selected for presentation also give good support to the validity of the decision to continue the sectional programs.

The program was initiated by a report from Pearson et al. of U.C.L.A. on an enzymatic deficiency present in a patient with McArdle's syndrome. Rudi Schmid initiated the discussion and presented information about another patient on the basis of data derived by different techniques but leading to similar conclusions. These data appear to establish an anomaly in muscle phosphorylase activity as the fundamental defect in this rare but striking disease. A word of caution was added by Perkoff's comment on a patient with similar clinical manifestations in whom an abnormality of phosphorylase was excluded.

After this propitious beginning, discussion waxed hot at times but waned to a desultory pace at other times. There seems little need to attempt to analyze the mechanisms involved after Ivan Bennett's clear presentation of the problem in his Presidential Address of last year. Certainly, the hope of a maximum of productive criticism was not attained in all instances. This may be due to the fact that within this section a con-

siderable variety of subjects was presented, ranging from muscle disease to clinical endocrinology, from metabolism and control of hormones to influences on carbohydrate and fat metabolism.

Another feature of the meeting not at all peculiar to this section was the excellent quality of the great majority of the presentations. It is my impression that, on the average, both the illustrative material and the clarity of description of experimental procedures have improved as compared with those of a few years ago. Although this is an ancillary problem, it is a commendable direction of change which should be nurtured. My most serious criticism would be of the lack of spontaneity which is apparent when the speaker reads extensively or entirely from a manuscript. In general, interest is better maintained if the final presentation, particularly of data on projected slides, is made without manuscript even at the risk of omission and grammatical error.

In spite of these limitations, the section accomplished its purpose of allowing many more presentations and wider discussion than would have been possible without the sectional programs. I must conclude that the sectional programs have a great deal of merit, although my personal prejudice has not been sympathetic to this development in our meetings.

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## Section III

The section dealing with renal and electrolyte physiology, met in the Rutland Room. The session was notable for free and vigorous discussion despite the fact that the room was somewhat overcrowded.

Oken, Whittembury, Windhager, Schatzmann and Solomon reported the results of studies of sodium transport by the proximal tubule of *Necturus*. Fluid instilled in blocked proximal tubules was analyzed and movements of water and sodium calculated. Measurements of transtubular potential differences were also performed. The results show net transport of sodium against the electrochemical potential gradient and indicate that an active process is involved. The high level of flux into the lumen (80% of the outward movement) indicates either a relatively high permeability to sodium ion or a considerable element of exchange diffusion. These observations, al-

though obtained in a different animal, are strongly opposed to the proposal of Malvin and his associates that electrolyte reabsorption in the proximal tubule is a passive process.

Studies of the effect of neurohypophyseal hormones on the permeability of toad bladder were reported by Lamdin, Maffly, Hays and Leaf. The techniques used were those of Ussing and his associates and for the most part the results with the bladder duplicate those obtained by Ussing with toad skin. The one striking and unexplained discrepancy involves thiourea. Vasopressin produced no increase in permeability to thiourea in the bladder preparation whereas a marked change had been observed with skin. On the other hand, the increase in permeability to acetamide and water are in agreement with Ussing's observations and his hypothesis that the effect is attributable to the opening of aqueous pores. These studies indicate that the permeation of urea is similarly affected and that the critical resistance modified by the hormone is at the mucosal boundary of the cells.

I. L. Schwartz, Fong, Popenoe, Silver and Schoessler have used tritiated vasopressin to investigate the nature of the attachment of vasopressin to its receptor sites in the kidney. They have found it firmly bound to the insoluble portion of kidney homogenate, and that it is released from this binding to any considerable extent only by conditions which yield reduction of disulfide bonds. The results suggest that the binding involves two disulfide bridges between hormone and receptor and several interesting possible models were proposed involving distortion of the configuration of the receptor as it combines with hormone.

The effects of the chronic administration of vasopressin in oil to subjects on a fixed water intake were reported by Jaenike and Waterhouse. The sodium and chloride loss which has been previously described was shown to be limited to the early phase of the regimen. The subjects then came into balance with respect to both salt and water. A striking, and unexplained phenomenon underlies the return to water balance: namely, a marked functional impairment of the ability to produce hypertonic urine. The lively discussion of this study centered around its implications to "salt-wasting" syndromes which have been attributed to "inappropriate" secretion of antidiuretic hormone. It would appear that the salt loss in such instances should be limited and a steady state achieved with some degree of dilution

and salt depletion. The subsequent paper of Carter, Rector and Seldin dealt with several patients with cerebral injuries in which salt loss was attributed to excessive antidiuretic hormone secretion in response to small decreases in extracellular fluid volume.

Handler presented studies in which the low urate clearance of pregnant women was shown to be correlated with elevation of the arterial blood lactate concentration. The author refrained from taking a stand on the nature of the interesting lactate effect on urate excretion—whether due to enhanced reabsorption or inhibition of the secretory mechanism which has been proposed by Gutman and his associates.

Investigations of magnesium excretion employing stop-flow analysis were reported by Murchugh and Robinson, and indicated that reabsorption occurred in the proximal tubule and that  $Mg^{28}$  appeared in distal samples when injected during stop flow. To investigate the latter an ingenious procedure was applied in which stop flow was interrupted to permit fluid which had been held in the proximal segments to move to the distal tubules for an additional period of stop flow. The results seem to favor exchange of Mg rather than secretion as the basis of the appearance of  $Mg^{28}$  in the distal segments.

The appearance of a weak acid in the distal, acidified samples of urine after flow was stopped by either arterial or ureteral clamping was reported by Brodsky, Kaim and Carrasquer. Although this acid could account for a major part of the observed acidification, the actual bicarbonate loss from the samples and the total amount of acid were small. Its occurrence with both arterial occlusion and ureteral stop flow suggested to the authors that there is anoxia of the renal papilla in ureteral stop flow, but the alternative, that the appearance of the weak acid is not related to anoxia in either instance, must also be considered.

The final paper of the afternoon program (W. B. Schwartz, Lemieux and Falbriard) dealt with the relationship between plasma bicarbonate concentration and bicarbonate reabsorption by the renal tubules in respiratory alkalosis. In this condition, as in the normal, reabsorption remains virtually complete until reabsorption is maximal, whereas in respiratory acidosis, as during carbonic anhydrase inhibition, bicarbonate appears in the urine long before reabsorption is maximal. Discussion centered around interpretation of the fact that in the latter situations the reciprocal of



reabsorption is a linear function of the reciprocal of plasma bicarbonate concentration. Opinion as to whether this indicates an essential participation of carbonic anhydrase in all bicarbonate reabsorption remains sharply divided.

The evening session of the Section drew almost to the capacity of the Rutland Room but discussion from the floor was noticeably less vigorous than in the afternoon session.

The program was opened with a description of the concentrating defect in sickle cell disease by Levitt, Levy, Hauser and Polimeros. The authors reported normal hemodynamic values and submaximal responses to administered ADH. Reduction in GFR by administration of a ganglionic blocking agent and the application of venous tourniquets did not induce a substantial rise in urine osmolality. It was proposed that this defect results from a failure to produce maximum medullary hypertonicity.

Franklin, Niall and Merrill presented their studies on the influence of solute load on the isosthenuria of renal disease. Solute load was reduced either by lowering of the GFR using ganglionic inhibitors or by reduction of plasma urea with dialysis. Despite reductions in osmolar clearance of more than 50% there was little change in osmolar U/P ratios with pitressin administration. It was suggested that the concentrating defect in these subjects may reflect a failure of the medullary concentrating system. The first two papers on the evening program as well as a number of those delivered in the afternoon reflected the current high degree of interest among renal physiologists in the details of the concentrating mechanism.

Robin, Bromberg and Forkner described a new method based on a familiar principle for estimating intracellular pH in vivo by making use of the dependence on pH of the ratio of  $\text{NH}_3$  to  $\text{NH}_4^+$ . Plasma  $\text{NH}_3$  content was evaluated by measuring alveolar  $\text{NH}_3$  tension after the intravenous administration of 0.2 M. ammonium acetate to dogs. During infusion of ammonium acetate, respiratory acidosis and alkalosis produced little change in the sum of blood  $\text{NH}_3$  and  $\text{NH}_4^+$ , while with metabolic acidosis there was a marked increase and with metabolic alkalosis, a fall. These results are in accord with the expectation based on the assumption that the metabolic alterations in acid-base balance involve mainly the extracellular fluid, the respiratory alterations both extracellular and intracellular compartments.

The paper which stimulated the most ex-

tended discussion from the floor was by Gill, Gann, Delea and Bartter on the correction of the defect in water excretion in untreated Addisonian patients by volume expansion alone. Evidence was presented indicating that the reduced free water excretion in the untreated patient was related to volume changes, and that volume expansion with either salt or albumin reversed the defect in the absence of replacement therapy with adrenal steroids. Much of the discussion centered on the possible role of ADH in this phenomenon.

The program closed with a paper by Valtin, Wilson and Tenney on the role of the left atrial stretch receptors in carbon dioxide diuresis. It was noted that pooling of blood in the extremities reverses the diuretic effect of  $\text{CO}_2$ , that hyperventilation without elevation of plasma  $\text{CO}_2$  tension does not induce a similar diuresis and that section of both vagi in cats does not abolish  $\text{CO}_2$  diuresis. The data seem to indicate that the left atrial receptor is not the sensing device responsible for  $\text{CO}_2$  diuresis. The effects of blood pooling may be related to a lowering of cardiac output and GFR. The possibility that  $\text{CO}_2$  diuresis is mediated via effects on the central nervous system and the hypothalamus in particular remains to be explored.

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## Section IV

*(The report of the meeting of the hematology section will be published in the November issue.)*

## Section V

The section on infectious diseases met at 2:30 p.m. on May 3, 1959, in the West Room. The room was filled to overflowing. The chairman, having received assurances through the year that infectious diseases were *déclassé*, if not entirely *passé*, was tempted to open with a macabre greeting to those who had gathered to pay homage to a dead subject.

The program reflected many of the current interests in infectious diseases.

Z. A. Cohn and S. I. Morse of New York, were displeased with earlier evidence that sug-

gested that virulent strains of *S. aureus* differed from avirulent strains not so much in resistance to phagocytosis as in resistance to intracellular bactericidal activity. These authors prepared suspensions of polymorphonuclear leukocytes to which equal numbers of staphylococci were added (in contrast to the usual experiments in which the bacteria are present in great excess). Avirulent coagulase negative staphylococci were phagocytosed rapidly and killed, whereas virulent coagulase positive organisms resisted phagocytosis. In the presence of immune serum, phagocytosis of virulent strains was greatly accelerated and the ingested organisms rapidly became non-viable. These experiments are in some conflict with earlier ones from other laboratories. It would appear that the chief differences between these and the earlier experiments lie in the differing ratio of bacteria to leukocytes in the experimental design. Probably, the present studies are a little closer to the natural order of things, although it would be useful to know more about the dynamics of phagocytosis and bacterial killing in experimental lesions.

The burgeoning interest in infections of the urinary tract, and increasing recognition of the role of bacteriuria in symptomatic and asymptomatic infections, has led A. I. Braude, of Pittsburgh, into the search for a rapid means for detecting bacteriuria. He has suggested the detection of catalase, since this enzyme is produced by the common pathogens of the urinary tract, other than enterococci. The enzyme is also produced by granulocytes and by the epithelium of the urinary tract. It is, therefore, apparent that its value as a possible screening agent for bacteriuria will be limited by the likelihood that injury to the urinary tract without bacteriuria will give positive tests for catalase. The data presented bear this out, and the detection of catalase in the urine must, therefore, be regarded as indicating injury to the urinary tract, with or without bacteriuria. Only a large scale clinical trial can determine the ultimate usefulness of this approach but it warrants further exploration.

R. S. Farr and F. J. Dixon of Pittsburgh continued the exploration of the dynamics of antibody formation that has been going on in their laboratories. They were here concerned with the detection of the minimal amount of antigen necessary to initiate antibody synthesis. They used iodine-labeled bovine serum albumin as the

antigen, and sought the antibody response in a variety of ways such as immune elimination, ability of animals to produce an immune response to a second challenge, etc.

Antigen concentration in the adjuvant mixtures given locally and in the plasma after an intravenous injection of the antigen were compared. The minimal concentration of antigen necessary to initiate an antibody response was about 0.1  $\mu$ g. of albumin nitrogen per ml. Larger amounts of antigen given in divided doses at several sites were less effective than higher concentrations given at a single site. Thus, the concentration of antigen presenting to antibody forming cells is more critical to the initiation of the specific synthetic response than is the total amount of injected antigen.

H. R. Holman, H. R. G. Deicher and H. G. Kunkel of New York have continued the attempts to elucidate the nature of the extraordinary antinucleoprotein activity of the sera of patients with systemic lupus erythematosus (see also the paper by H. C. Goodman read during the morning session). The sera of patients with S.L.E. have been shown to react to varying degrees, not only with isolated cell nuclei and nuclear nucleoprotein, but also with fractions extracted from nuclei and separable from nucleoprotein, DNA or histone. Such broader reactions have been detected also in sera from patients with scleroderma, rheumatoid arthritis and other chronic illnesses. Serum factors have also been detected which react with DNA alone, or with histone alone. The L.E. phenomenon depends on the serum reaction with DNA plus histone, hence the serum factors reacting with these components alone, or with the other constituents of nuclear extracts do not produce the L.E. phenomenon. At present, no clear pattern of interrelationship of the "antigens" to one another or to the antibody-like factors in the sera has emerged, but it is apparent that important and fundamental knowledge of autoimmune phenomena is emerging from the studies of this disease process.

Along related lines are the observations of A. R. Hennes, R. L. Carpenter, M. Moore and J. F. Hammarsten, of Oklahoma City. Saline homogenate of human lung was absorbed on to latex particles and used as an antigen. Sera from a small group of controls were not reactive with these particles, but sera from many patients with tuberculosis and with emphysema had a reactive

substance to the latex particles so coated. The nature of the antigen in lung is not clear, but extracts of other tissues did not react with the sera that reacted with extracts of lung. It will be of importance to determine the nature of the reaction. Ordinary morphologic and clinical evidence argues against an autoimmune basis for these observations, but our knowledge of autoimmune phenomena in disease is undergoing such a revolution that a priori conclusions are hazardous.

G. G. Jackson, H. F. Dowling and W. J. Mogabgab of Chicago undertook a detailed investigation of two viruses, 2060 and J. H., that have been implicated in the etiology of the common cold. These viruses were cultivated in monkey kidney cell tissue cultures and given in large doses to human volunteers. An afebrile coryzal illness was produced in 25-34% of volunteers and occurred in 18% of controls. Those who recovered from infection with one virus were immune to the other. The two agents, isolated independently from coryzal illness, seem to be immunologically closely related or identical.

H. B. Houser of Cleveland has been studying systematically the usefulness of gamma globulin as a prophylactic agent in viral diseases. In this study, recruits in an Air Force base were found to have significantly fewer hospital admissions from respiratory illness after prophylactic administration of gamma globulin when compared with recruits receiving saline alone. Although some question about the adequacy of the placebo might be raised, the findings are strongly suggestive of a protective effect, and, of course, bear evidence of the high rate of adenovirus infection in the general population from which the globulin was obtained.

I. Tamm of New York has made the interesting observation that 2-(alpha-hydroxybenzyl)-benzimidazole selectively inhibits the multiplication of type 2 poliovirus in monkey kidney cultures, but does not influence influenza B virus. The inhibitory substance also does not produce much visible damage to the tissue culture cells. Thus, a pathway is blocked that is needed for the proliferation of poliovirus, but not for influenza virus.

In conclusion, the chairman wishes to acknowledge with appreciation the contributions of many of the audience to the lively and rewarding discussions that followed almost every

paper. It is evident that the phenomena of infection and immunity continue to fascinate lively minds.

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## Section VI

The section on the gastrointestinal tract and the liver met in the Music Room of the Chalfonte Hotel. Nine papers were presented, five having been submitted to the American Federation for Clinical Research, and four were selected from abstracts submitted to the American Society for Clinical Investigation. It is probably significant of current trends that of these nine papers seven dealt with the gallbladder and the liver and only two with the remainder of the gastrointestinal tract. A large and attentive audience remained throughout the entire three hour program. The absence of those periodic mass migrations which characterize the larger national meetings was particularly refreshing. The auditors of the subsection meeting with their delimited interests are apparently prepared to stay with the subject matter. This in itself, I believe, is a very potent argument for the desirability of continuing these subsection meetings.

Solomon, Lewinter and Spiro presented further evidence that glucagon inhibits the gastric secretion of acid and pepsin by a mechanism which is entirely inexplicable at present, but obviously is not related to hypoglycemia.

Jacobson, Chodos, Prior and Faloan have produced an experimental malabsorption syndrome in man by the antibiotic neomycin. The spirited discussion which followed indicated the audience's appreciation of the potentiality of this experimental malabsorption study.

Smith and Giles presented a preliminary report on the carbohydrate chemistry of bile in relation to stone formation.

Wheeler and Ramos studying bile secretion in the dog formulated a two component hypothesis which will undoubtedly be a takeoff point for future study.

Rapaport, Ketterer and Wiegand presented their material on the hepatic clearance of the new green dye. Discussion of this paper by Leevy, as well as the paper itself, indicated that this dye

may find a place in the study of hepatic blood flow.

The conjugation of bromsulphalein is an area of much current research activity. Javitt, Wheeler, Baker and Ramos presented their evidence that bromsulphalein is conjugated with glutathione. The discussion by Carbone and Coombes, both active workers in their field, was probably the highwater mark of this session.

Stormont and Mackie presented an abnormality in NEFA metabolism in cirrhosis.

Owen, Flanagan, Berry and Tyor returned to the problem of blood ammonia in liver disease, suggesting that the kidney was an important

source of augmented blood ammonia under the influence of diamox.

Mc Collum and Isacson presented a very critical and temperate account of the current status of the hemagglutination test in liver disease.

By limiting the program to nine papers, thus allowing twenty minutes for presentation and discussion of each, there was ample time for comment and question by the audience which allowed for a leisurely pace and encouraged full exchange of opinion.

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## Acknowledgment

It is the primary purpose of the AMERICAN FEDERATION FOR CLINICAL RESEARCH to provide an opportunity for young investigators in the medical sciences to take part in scientific meetings and to present and publish the results of their work. In order to attain this goal, it has been necessary to maintain the dues of the organization at a modest level which does not place a burden upon men with residency or fellowship status. For years, therefore, the Federation has financed its meetings and publication in part by the generous support of various companies which manufacture drugs, pharmaceuticals and scientific apparatus.

In recognition of the valuable assistance which these concerns have given to the Federation, the Council, at its annual meeting in May, 1954, established the categories of Sponsoring, Supporting and Contributing Membership. The officers wish to take this opportunity to acknowledge the liberal help given to the Federation by the following concerns in 1959.

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